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**METABOLIC CHANGES IN HUMANS
FOLLOWING TOTAL BODY IRRADIATION**

REPORT PERIOD

May 1, 1963 to February 29, 1964

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ABSTRACT

These studies are designed to obtain information which is necessary to estimate combat effectiveness of troops and to develop methods of diagnosis, prognosis, prophylaxis and treatment of radiation injury. At the present time parameters of active investigation are clinical findings, hematologic effects, profile scores, miscellaneous laboratory tests, deoxycytidine excretion in the urine, xanthurenic acid excretion in the urine, chromosome changes in leucocytes, immunologic studies and the use of autologous bone marrow.

Six patients were given from 149r to 231r (100-150 rad) total body irradiation from a Co⁶⁰ source. Only one of the patients had prodromal nausea and vomiting with nausea lasting 48 hours. The lowest hematologic values were found 25 to 35 days after irradiation.

Deoxycytidine was found in increased amounts in the urine from patients after total body irradiation. In rats much larger amounts were found in the urine after 500r and 800r whole body irradiation than after lesser doses.

Studies by Dr. Anthony Luzzio, U.S. Army Research Laboratory, Ft. Knox, Kentucky, indicate there may be an immunologic post irradiation alteration in human gamma globulin antigenicity.

Combat effectiveness would be relatively maintained with an exposure up to 200 rad, though a second exposure would result in significant troop ineffectiveness.

Animal experiments described herein were conducted according to the principles of laboratory animal care as promulgated by the National Society for Medical Research.

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I. INTRODUCTION

This project was initiated in February 1960 and this report presents data accumulated from May 1, 1963 through February 29, 1964. The previous reports of November 1961 and April 1963 (DASA 1422) cover the data compiled prior to May 1963.

Six additional patients have received from 149 r to 231 r (100-150 rad) total body irradiation in the period covered by this report.

2. AIMS AND SCOPE OF THE PROJECT

These studies are designed to obtain new information about the metabolic effects of total body and partial body irradiation so as to obtain a better understanding of these acute and subacute effects in human beings. This information is necessary to provide knowledge of combat effectiveness of troops and to develop additional methods of diagnosis, prognosis, prophylaxis and treatment of these injuries.

At the present time parameters of active investigation are:

1. Clinical findings
2. Hemograms and profile scores
3. Miscellaneous laboratory tests (serum urea nitrogen(SUN), blood cultures, C-Reactive Protein and bone marrow aspiration)
4. Deoxycytidine and other nucleosides in urine
5. Xanthurenic acid in urine
6. Chromosome changes in white cells
7. Quantitative precipitin test (Dr. Luzzio, U.S. Army Medical Research Laboratory, Ft. Knox, Kentucky)

8. Levels of serum lipoproteins (Lt. Col. E.C.

Knoblock, Walter Reed Army Institute of Research)

9. Use of autologous marrow

3. SELECTION OF SUBJECTS

Only patients with metastatic or incurable neoplasms are eligible for such studies. Patients who have solid tumors which might be radioresistant are sought. Relatively good nutritional status, normal renal function and a stable hemogram are required. Interpretation of the effect of the underlying disease on the observed metabolic changes remains a problem.

Patients who have had no previous radiation or chemotherapy are generally used though some patients so previously treated have been studied. It is possible to isolate the effect of previous radiation by such studies.

4. TECHNIQUE OF STUDY

The design of the study is such that the patient serves as his own control. A pre-irradiation control period of one to two weeks is utilized. However, with the increased levels of radiation, the post-irradiation period has been extended to six or eight weeks.

Five observations are made in the pre-irradiation period. Observations currently made are listed in Table I. Post irradiation specimens are then obtained at standard test times as described by Thoma and Wald (See section on Analysis of Data).

Patients have been studied on the Tumor Ward and the Metabolic Ward of the General Hospital. One bed on the Metabolic Ward has been allotted for this study.

During the pre-irradiation period, the patient's records are reviewed by the physicians to be certain that the contribution of the underlying disease can be evaluated. One or two sham irradiations are given to permit accurate dosimetry and obtain cooperation by the patient. There is no discussion of possible subjective reactions resulting from the treatment. Other physicians, nurses, technicians and ward personnel are instructed not to discuss post-irradiation symptoms or reactions with the patient.

5. ANALYSIS OF DATA

Collection of data continues essentially according to the plan of Thoma and Wald (J. Occup. Med. 1:420-447, 1959) and described in section 3 of Medical Aspects of Radiation Accidents, E.L. Saenger, ed., U.S. Government Printing Office, 1963, (Table I).

All data are recorded on score sheets and then transferred to IBM cards. Thus all information together with the appropriate machine programs is available for analysis by other centers or interested individuals.

Profile scoring is used to estimate the effect of previous irradiation or chemotherapy. The method is described in Appendix B of DASA 1422.

6. DOSIMETRY

The methods of dosimetry remains the same as in the report of April 1963. The dosimetry for the patients is given in Table II.

7. CLINICAL OBSERVATIONS

Six additional patients have been studied since the last report. They received from 149 to 231r of total body radiation (total midline dose in air without a phantom). Clinical summaries are attached to this report as Appendix A. Patient #032 received only sham because of a low white count and hypoplastic

marrow when checked in the pre-radiation period. Patient #034 was abandoned due to progression of her disease.

One (#031) of the patients irradiated had radiation to her uterus thirty-four years prior to total body irradiation. One patient (#030) had received a piperazine derivative (A8103 - Abbott) eight months before total body radiation. The four other patients were untreated.

Only one of the patients had prodromal symptoms of nausea and vomiting with persistence of nausea to 48 hours after a dose of 227 r (150 rad). She had received no previous therapy.

As has been seen before, there appeared to be increased lassitude. Quantitation of this observation will require specific procedures for performance testing.

8. HEMATOLOGY AND PROFILE SCORING

The presence of a "plateau" or "peak" in the white blood cell count has continued to be observed. It is noted at approximately ten days and continues until about the twentieth day. The lowest hematologic values are observed between the twenty-fifth and thirty-fifth day after radiation.

Mild lymphocytopenia was seen on the treatment day. Occasional giant polymorphonuclear granulocytes were seen in two patients.

Profile scoring was continued in the same manner as described in the Summary Report of April, 1963, Appendix B. Delineation of disease score, radiation score and total continued to be of value in ascribing the importance of radiation in precipitating demise. "Net erythrocyte" score was again used. In this group of patients "net erythrocyte" score did not introduce significant change from a score based on the hematocrit. Table III summarized the data based on

profile scoring.

9. DEOXYCYTIDINE

Four additional patients have been evaluated in regard to urinary excretion of deoxycytidine (dCT). This substance was found in increased yields in the post radiation phase for periods up to 48 hours, (See Table IV). It is apparent from the first six patients that we have not as yet demonstrated a dose effect relationship. The lack of such a relationship probably represents difficulties with the technical procedure although it may be due to effect of concomitant disease. Because of the wide confidence limits noted in several of our concurrent rat experiments we suspect that the problem is a technical one.

Four patients who have not received radiation but who had other illnesses have been studied for urinary dCT excretion. These conditions included thermal burn, fracture, infection and cancer. None showed dCT. The only human so far studied who has shown urinary dCT is patient #030 who had received chemotherapy with A 8103 (Abbott) about 8 months prior to irradiation. The observation that dCT is not excreted in at least a few other disease states indicates that its excretion may at least be relatively specific for radiation.

Some experiments have been carried out using the Wistar rat. Groups of 12 male rats were exposed at doses of 0, 200, 500 and 800 rad. Rats excrete some dCT normally and pre-radiation levels ranged 10 ± 100 $\mu\text{g}/24$ hours, (Table V). All rats showed an increase in deoxycytidine excretion post radiation. The rats exposed at 500 rad showed an increase over those receiving 200 rad. There was no significant difference between dCT levels at 500 and 800 rad.

Laboratory techniques for dCT analysis in urine have been quite tedious and have not as yet reached the desired degree of accuracy. The entire procedure is being re-evaluated to develop a method by which larger numbers of specimens can be assayed in shorter times.

10. QUANTITATIVE PRECIPITIN TEST

Serum from our patients has been stored and sent to Dr. Anthony J. Luzzio of the U.S. Army Medical Research Laboratory, Ft. Knox, Kentucky. The serum has been examined for radiation altered human serum gamma globulin. (Luzzio, A.J. The Serologic Specificity of Radiation Altered Human Serum Gamma Globulin, The Journal of Immunology, 90:224, Feb., 1963). Serum from several patients showed a bimodal post irradiation increase in this material (Fig. 1). These data suggest an alteration in antigenicity of human serum gamma globulin as a result of in vivo irradiation.

11. CHROMOSOME STUDIES

Observation of peripheral blood chromosome cultures has continued. A finding of particular interest has been the observation of endoreduplication. This phenomenon has been observed in eleven patients with cancer and in one control. It has been seen before and after irradiation. Four patients have been studied in detail (Table VI). In at least one patient increased incidence of this occurrence seems to be a radiation effect. At this time it is not clear whether this observation is associated with irradiation or the presence of malignancy. Additional studies are being carried on in controls and patients with malignancy to evaluate further the role of irradiation.

12. STATISTICS

Computer analysis of the hematologic data on the first twenty-nine patients has started. The patients have been divided into four groups:

- 1) Those receiving 100 rad or less total body irradiation who have not had previous irradiation;
- 2) those receiving 100 rad or less total body irradiation who have had previous irradiation;
- 3) those receiving more than 100 rad of total body irradiation who have not had previous irradiation;
- and 4) those receiving more than 100 rad of total body irradiation who have had previous irradiation.

Printouts of each group and of the combined groups for each parameter were constructed with the abscissa in days post irradiation. On the ordinate the means of the pre-irradiation values were standardized at unity (1). Therefore all post irradiation values were related to the mean of the pre-irradiation observations (Fig. 2 is a representative printout).

A fall in hemoglobin, hematocrit and reticulocytes in patients who received more than 100 rad total body irradiation was observed. Previous therapy seemed to influence the immediate lymphocyte fall and later decrease in monocytes of the high dose patients. Total white cells in the peripheral blood decreased in all groups but to a greater extent in patients given more than 100 rad who had received previous irradiation.

13. PROPOSALS FOR HUMAN STUDY PROGRAM

We propose to continue observing clinical and hematologic effects of irradiation with a Co-60 unit at a rate of approximately 5.4 r/min at 282 cm. Exposures will be total and partial body, bilateral and unilateral. Storage and

reinfusion of autologous bone marrow will be accomplished in the facility which has been established.

The determination of urinary excretion of deoxycytidine, chromosome changes and immunologic alterations will continue. Further exploratory investigations of performance testing will be made.

Preliminary discussions regarding studies in volunteers will be instituted. These will, of necessity, require considerable perspicacity and contemplation. However, it is our hope such a program will be feasible.

a) Clinical and hematological observations of cobalt 60 irradiation at dose rates of 5.4 r/min at 282 cm. will continue. Exposures will be given to the whole body, partial body (upper and lower portions and unilateral).

Facilities for storage and reinfusion of bone marrow are just being installed. Trials on cadavers will be made for the next four months after which marrow storage will be carried out on subjects. The purpose of marrow storage and reinfusion is to protect subjects who receive doses in excess of 150 rad in the event of bone marrow failure. We hope to utilize doses between 200 - 300 rad.

b) Deoxycytidine studies - The assay of urinary deoxycytidine will be re-evaluated so as to simplify the techniques as discussed above.

The most interesting aspect of dCT is the mechanism of urinary excretion. In order to attempt to clarify this problem further the following studies with C-14 labeled and tritiated materials are planned:

- 1) Clearance from blood
- 2) Determination of the existence of a renal threshold
- 3) Measurement of a respiratory component of C-14 labeled dCT (i.e. C¹⁴O₂).

These experiments will not, of course, answer the question posed previously as to whether dCT is produced because of interference with synthesis or because of increased breakdown of nuclear DNA. But until the metabolism of dCT is better understood in the human being, the elucidation of this problem by the administration of labeled precursors of dCT cannot be undertaken.

Initially the method of breath analysis for $C^{14}O_2$ using the Carey vibrating reed electrometer will be undertaken with C^{14} labeled glucose and glycine in order to develop the methodology at a lower cost.

The initial labeled dCT will be labeled in the 2 position of the pyrimidine ring. Subsequently uniformly labeled tritiated material will be used. These studies will be carried out in patients other than those receiving whole body irradiation. Later studies in succeeding years envision the administration of DNA precursors for the labeling of dCT in irradiated humans.

c) Immunological studies continue with plasma samples being sent to Dr. Luzzio at the U.S. Army Medical Research Laboratory, Ft. Knox, Kentucky.

PUBLICATIONS

Deoxycytidine in Urine of Humans after Whole-Body Irradiation, Helen K. Berry, Eugene L. Saenger, Harold Perry, Ben I. Friedman, James G. Kereiakes and Carolyn Scheel.; Science, Vol. 142, No. 3590, pages 396-398, October 18, 1963.

SUMMARY

1. Six additional humans with cancer have received 149-231 r (100-150 rad) total body irradiation.
2. Deoxycytidine has been found in increased amounts in the urine from patients following whole body irradiation. Much larger quantities of deoxycytidine have been found in the urine of rats after 500 r and 800 r whole body irradiation than after lesser doses.
3. The observation of endoreduplication in the peripheral blood chromosome preparations may be related to malignancy but was increased following total body irradiation.
4. Studies by Dr. Anthony Luzzio, U.S. Army Research Laboratory, Ft. Knox, Kentucky, indicate there may be an immunologically distinct bimodal post irradiation alteration in human gamma globulin antigenicity.
5. Computer analysis of data from the first 29 patients irradiated suggests a fall in the hemoglobin, hematocrit and reticulocytes in patients receiving more than 100 rad total body irradiation. The immediate fall in lymphocytes and later fall of monocytes in patients receiving more than 100 rad seemed associated with previous therapy. Total white cells decreased in all groups but to a more striking degree in patients who had previous therapy and were given a high dose.
6. Combat effectiveness would be maintained relatively well with an exposure up to 200 rad. However a second exposure would probably result in significant troop ineffectiveness.

TABLE I

PRE AND POST IRRADIATION OBSERVATIONS

1. Complete history and physical examination
2. Temperature, pulse, and respiration
3. Body weight
4. Medications - fluids, antibiotics, steroids, narcotics
5. Hematology - Hgb., RBC, WBC, differential, hematocrit, platelets,
reticulocytes, erythrocyte sedimentation rate
6. Urine
 - a) volume
 - b) routine urinalysis
 - c) chromatography for deoxycytidine
 - d) chromatography for xanthurenic acid
7. Serum urea nitrogen
8. Lipoproteins
9. Quantitative precipitin test
10. Chromosome studies
11. Blood cultures
12. C reactive protein
13. Bone marrow aspiration

TABLE II

TOTAL BODY RADIATION DOSIMETRY

<u>Patient No.</u>	<u>Midline Air Dose Roentgens</u>	<u>Midline Tissue Dose Rads</u>
030	149	100
031	155	100
033	152	100
035	227	150
036	153	100
037	231	150

TABLE III

PARTITION OF PROFILE SCORES BASED ON
"NET ERYTHROCYTE" SCORE

<u>Case No.</u>	<u>Disease Score</u>		<u>Radiation Score</u>		<u>Total Score</u>	
	<u>Test</u>	<u>Cumulative</u>	<u>Test</u>	<u>Cumulative</u>	<u>Test</u>	<u>Cumulative</u>
030	0.8	16.0	0.5	34.0	1.3	50.0 (89)
031	2.0	41.2	0.0	1.1	0.0	42.3 (89)
033	1.4	25.2	1.3	27.1	2.7	52.3 (61)
035	0.0	00.0	1.0	95.7	1.0	95.7 (61)
036	1.4	24.1	4.6	100.2	6.0	125.3 (47)
037	1.0	10.0	11.7	33.7	12.7	47.7 (26)

() = Days post radiation

032 and 034 did not receive radiation

TABLE IV

DEOXYCYTIDINE EXCRETION IN HUMANS

<u>Pt.</u>	<u>Age</u>	<u>Sex & Race</u>		<u>Diagnosis</u>	<u>Dose (rad)</u>	<u>Total dCT (mg)</u>
027	17	M	W	Ewing's Sarcoma	150	182
029	63	F	W	Ca. Breast	150	52
030*	54	M	NW	Ca. Stomach	100	66
031	81	F	NW	Ca. Breast	100	25
033	64	M	NW	Ca. Colon	100	30

* Rec'd A-8103 pre rad. Had 8 mg. dCT pre rad.

TABLE V

URINARY EXCRETION OF DEOXYCYTIDINE IN TOTAL BODY

X-IRRADIATED RATS

<u>Urine Collection Period</u>		<u>Deoxycytidine Levels (µg/rat)</u>			
		<u>0 r</u>	<u>200 r</u>	<u>500 r</u>	<u>800 r</u>
Pre -	24 hours	42 (0-90) *	20 (0-60)	18 (0-70)	30 (0-100)
Post	0-24 hours	62 (36-120)	484 (248-585)	1755 (630-3050)	1611 (1056-2660)
	24-48 hours	39 (0-100)	97 (50-130)	118 (15-225)	236 (66-450)
	48-72 hours	19 (0-48)	62 (10-110)	70 (0-130)	114 (10-280)

* numbers in parenthesis indicate range of values.

TABLE VI

INCIDENCE OF ENDOREDUPPLICATION

(Patients)

<u>S.H.</u>	<u>Chromosome Sampling Date</u>	<u>Cells Showing Endoreduplication</u>	<u>No. of Mitosing Cells Counted</u>	<u>Incidence %</u>
	11/15/63	0	2272	0.00
	11/18/63	0	1874	0.00
	11/22/63	0	3208	0.00
11/24/63 100 Rad Total-Body Irradiation				
	11/24/63 2 hr post irradiation	0	2029	0.00
	11/24/63 6 hr post irradiation	0	3920	0.00
	11/25/63	8	1401	0.57
	11/29/63	0	2180	0.00
	12/6/63	0	1619	0.00
	12/13/63	0	1522	0.00
	12/20/63	0	2068	0.00
	12/24/63	1	2015	0.05
<u>M.R.</u>	10/18/63	0	1942	0.00
	10/23/63	1	2500	0.04
	10/25/63	0	1604	0.00
10/27/63 150 Rad Total Body Irradiation				
	10/27/63 2 hr post irradiation	2	1862	0.11
	10/27/63 6 hr post irradiation	1	563	0.18
	10/28/63	1	1425	0.07

TABLE VI
(continued)

<u>Chromosome Sampling Date</u>	<u>Cells Showing Endoreduplication</u>	<u>No. of Mitosing Cells Counted</u>	<u>Incidence %</u>
<u>M.R. (continued)</u>			
11/1/63	0	1383	0.00
11/8/63	0	3873	0.00
11/15/63	0	1372	0.00
11/22/63	0	3073	0.00
11/26/63	0	3633	0.00
<u>F.W.</u>			
3/8/63	17	12743	0.13
3/11/63	0	1966	0.00
3/14/63 pre-irradiation	4	1993	0.20
3/14/63 150 Rad Total Body Irradiation			
3/14/63 post-irradiation	74	7979	0.93
3/15/63	1	59	1.69
3/20/63	0	48	0.00
3/26/63	0	556	0.00
4/1/63	3	1281	0.23
4/8/63	1	2810	0.04
4/15/63	0	55	0.00
<u>M.L.</u>			
6/4/63	8	18196	0.04
6/11/63	2	1254	0.16
6/14/63	3	2788	0.11

TABLE VI
(continued)

<u>Chromosome Sampling Date</u>	<u>Cells Showing Endoreduplication</u>	<u>No. of Mitosing Cells Counted</u>	<u>Incidence %</u>
M.L. (continued)			
6/16/63 100 Rad Total Body Irradiation			
6/16/63 2 hr. post-irradiation	1	83	1.20
6/16/63 6 hr. post-irradiation	6	2928	0.20
6/17/63	11	3209	0.34
6/21/63	7	5115	0.14
6/28/63	0	1558	0.00
7/5/63	3	3260	0.09
7/11/63	2	2256	0.09
7/16/63	21	11774	0.18

APPENDIX A

CLINICAL SUMMARIES

Study No. 030

Patient J.D.

Chart No. 382572

This patient was a 54 year old Negro male who had a laparotomy performed on September 11, 1962. The operation revealed a carcinoma of the stomach which was inoperable due to widespread metastases to the celiac and middle pelvic nodes, the peritoneum and omentum. A gastrojejunostomy was performed. (CGH SP 62-2445). Following surgery, he had increased appetite and cessation of vomiting, but severe pain in the abdomen continued. He was discharged on September 27, 1962.

On October 9, 1962, he was placed on A-8103, 40 mgm/day, as well as medication for control of pain and gastric spasm. The chemotherapy was discontinued in December, 1962.

On May 17, 1963, the patient was admitted to CGH with complaints of nausea and vomiting of three weeks duration. A 10 cm. mass was present in the epigastrium.

The patient received 100 rad total body radiation on June 6, 1963. (Total absorbed dose at axis). The midline air dose was 149 r. He had no symptoms following treatment. The patient had some nausea and vomiting which was not related to his radiation therapy, but was associated with a partial obstruction at the operative stoma. Thirty days after treatment he developed leukopenia and thrombocytopenia with the leukocyte and platelet counts returning to pre-treatment levels by sixty days post radiation. A mild anemia developed approximately one

Study No. 030 (continued)

week after treatment and persisted through seventy-five days post radiation.

He subsequently received chemotherapy, but expired December 23, 1963. No autopsy was obtained.

Study No. 031

Patient M.L.

Chart No. 116158

The patient is an 81 year old Negro female who had the diagnosis of carcinoma of the right breast made in February, 1958. On March 7, 1958, a right radical mastectomy was performed. (CGH SP 58-391).

On May 14, 1963, the patient was admitted to CGH with a mass in the left breast which had been slowly increasing in size for one year. There was also a mass over the liver. Biopsy of the breast on May 23, 1963, revealed carcinoma of the breast (CGH SP 63-1301) and on May 28, 1963, a simple mastectomy was performed. (CGH SP 63-1379).

The patient had radiation therapy for fibroids thirty four years prior to the first breast amputation. She did not receive post-operative radiation therapy.

On June 16, 1963, the patient received 100 rad total body radiation. (Total absorbed dose at axis). The midline air dose was 155 r. She had no symptoms following treatment. Thirty days after treatment leukopenia and thrombocytopenia developed. The platelet count returned to pre-treatment levels by sixty days and the leukocytes by seventy-five days post radiation. Prior to treatment the patient had a mild anemia with the hemoglobin averaging 10.5 grams, the hematocrit 35%. Since treatment there has been improvement in the anemia, and seventy-five days post radiation her hemoglobin was 11.9 grams, hematocrit 38%.

The patient is being followed and has received local Cobalt 60 therapy.

Study No. 033

Patient A.J.

Chart No. 363128

The patient was a 64 year old Negro male who had the diagnosis of adenocarcinoma of the colon made in March, 1959. A colectomy and ileotransverse colostomy was performed March 24, 1959. (CGH SP 59-980).

On May 28, 1963, the patient was seen in Medical Clinic with complaint of weight loss and upper abdominal pain of several months duration. At this time the presence of a large right upper quadrant mass was noted and he was referred to Tumor Clinic.

The patient was admitted to CGH on June 24, 1963, for evaluation for total body radiation with a diagnosis of 1) recurrent carcinoma of the colon with metastasis to the liver, and 2) abdominal hernia. He had received no previous radiation therapy.

On July 7, 1963, he received 100 rad total body radiation. (Total absorbed dose at axis). The midline air dose was 152 r. He experienced no symptoms from radiation. Prior to treatment, the patient's major complaint was severe intermittent pain in the hepatic region. He had some slight relief from pain, and a slight decrease in size of the hepatic mass. Twenty-six days after treatment, the patient developed leukopenia and thrombocytopenia with the leukocyte and platelet counts returning to pre-treatment levels by thirty-nine days post radiation.

On August 6, 1963, the patient was discharged, but on August 20 he was readmitted with complaint of severe anorexia, nausea, weakness, and abdominal pain. His WBC rose to 17,000 and chest x-ray revealed pneumonia. His course continued downhill and the patient expired October 1, 1963. No autopsy was obtained.

Study No. 035

Patient M.R.

Chart No. 415556

The patient is a 53 year old Negro female who had the diagnosis of carcinoma of the right breast with metastases to the skin and right and left supra-clavicular nodes made in April, 1963. (CGH SP 63-952). She also had a large abdominal mass and on May 1, 1963, an abdominal hysterectomy for large uterine fibroids was performed. (CGH SP 63-1100).

On October 15, 1963, the patient was readmitted to CGH for evaluation for total body radiation. She had no previous radiation therapy or chemotherapy.

On October 27, 1963, the patient received total body radiation of 227 r (midline dose in air), which was equivalent to 150 rad (total absorbed dose at axis). Approximately two hours after treatment she complained of anorexia, nausea and vomiting, and "feeling lightheaded". The vomiting abated after approximately six hours, but anorexia and post prandial nausea persisted for forty-eight hours. The patient has also complained of weakness and fatigue since treatment but admitted, upon questioning, that she also experienced these symptoms prior to treatment. Hematological studies before treatment revealed average values of: Hemoglobin 12.4, hematocrit 41%, RBC 5,100,000, WBC 8,400, platelet 250,000. Seventeen days post treatment the blood values had fallen to: Hemoglobin 11.2, hematocrit 36%, RBC 4,200,000, WBC 3,800, platelet 166,000.

On November 20, 1963, 24 days post treatment, the patient's platelet count was 50,400. It continued to drop to a low of 36,560 thirty-six days post treatment. Between 28 and 47 days post treatment, guaiac positive stools and micro-hematuria were observed. By 54 days post treatment the platelet count

Study No. 035 (continued)

had returned to pre-treatment levels and upon examination 61 days post treatment the stool was guaiac negative.

The WBC reached its lowest point, 1100 cells/mm³, 33 days post treatment. It remained between 1100 and 2500 until 47 days post when it rose to 3,150. It continued to climb and 75 days post treatment the WBC was 7,450. Bone metastases were noted in February, 1964.

Study No. 036

Patient S.H.

Chart No. 301648

The patient is a 64 year old Negro male who was first admitted to CGH on November 12, 1954. A right colectomy was performed November 23, 1954 and the diagnosis of colloid adenocarcinoma of the colon was made. (CGH SP 54-2560). None of 20 lymph nodes were involved. The patient was readmitted to CGH on October 7, 1963 and on November 1, 1963 an exploratory laparotomy was performed which revealed sigmoid carcinoma, unresectable. A loop colostomy was performed and in addition a biopsy was obtained which revealed colloid carcinoma (CGH SP 63-2704).

The patient had received no previous radiation therapy. On November 24, 1963, 100 rad total body radiation was administered (total absorbed dose at axis). The air dose at the body mid axis was 153 r.

The patient tolerated the procedure well and experienced no symptoms following radiation. Prior to treatment, the patient's average hematology values were: hemoglobin 10.8, hematocrit 37%, WBC 6,400, platelets 250,000, reticulocytes 0.8%, sedimentation rate 50.

The patient's blood count reached a low at 26 days post radiation of: hemoglobin 9.5, hematocrit 30%, WBC 2,000, RBC 3.7, reticulocytes 0.5%, platelets 64,000, with an increase in uncorrected sedimentation rate to 57. At 44 days post treatment the count appears to be rising, but has not yet returned to pre-treatment levels. Progression of the underlying disease continues.

Study No. 037

Patient W.R.

Chart No. 424061

The patient was a 64 year old Negro male who was first admitted to CGH on November 19, 1963. Gastrointestinal series on November 19, 1963, revealed cardiospasm of the distal third of the esophagus, possible lesion of the cardio-esophageal junction, and grossly abnormal stomach wall, with changes consistent with carcinoma of the stomach. The diagnosis of metastatic signet ring carcinoma was confirmed by esophagoscopy November 22, 1963, and left scalene lymph node biopsy November 23, 1963. (CGH SP 63-2917). Due to the distant disease, 1) left scalene lymph node, 2) a definite evidence of Blumer's shelf, the patient was immediately worked up for total body radiation. The patient had no previous radiation therapy.

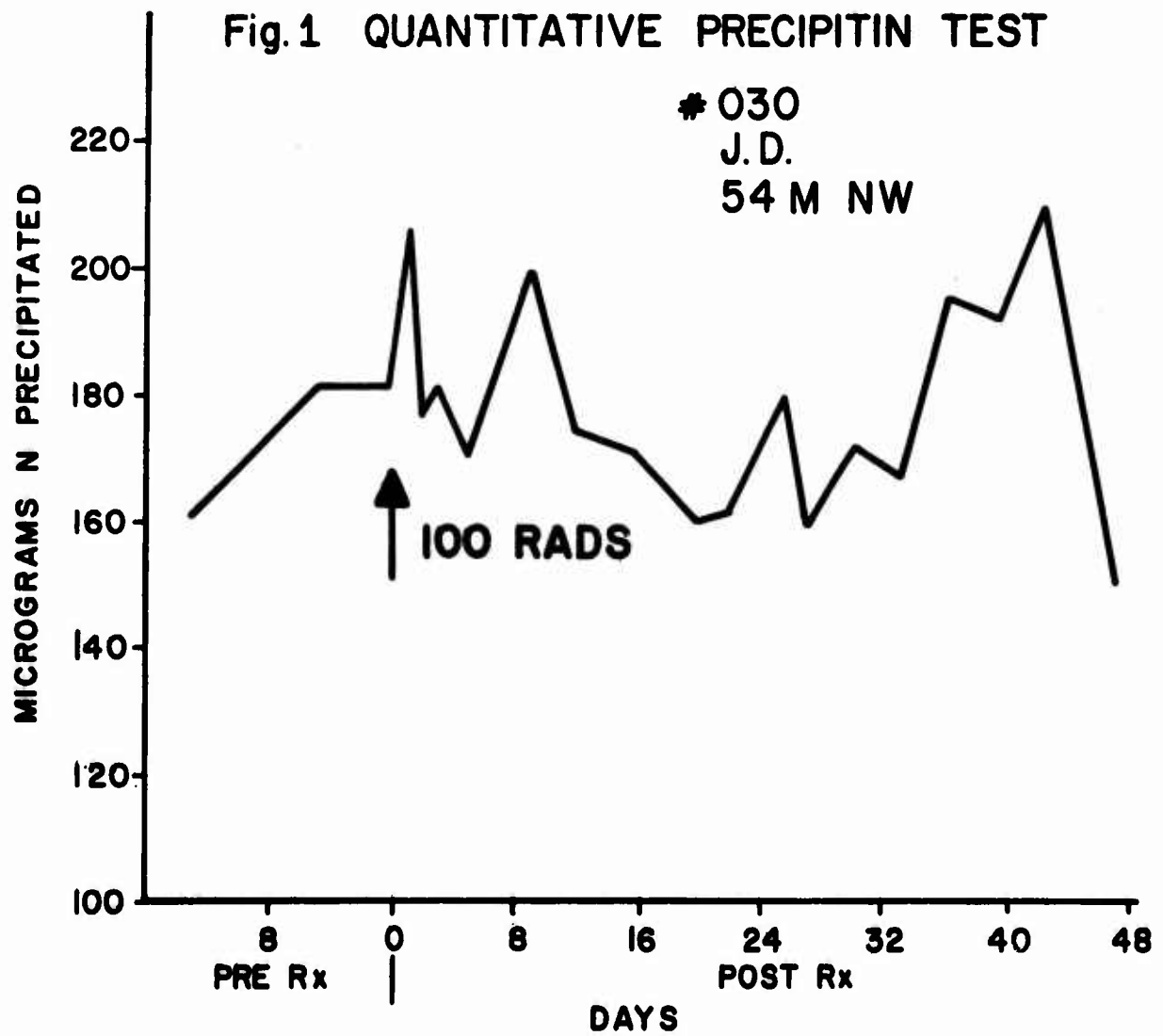
On December 15, 1963, the patient received 150 rad total body radiation (total absorbed dose at axis), i. e. , 231 r in air. He experienced no symptoms following radiation. Prior to treatment, the patient's average hematology values were: hemoglobin 12.3, hematocrit 37%, RBC 3.7 million, WBC 7,800, reticulocytes 0.7%, platelets 225,000, sedimentation rate 40 mm. By 23 days post radiation, the values had fallen to: hemoglobin 11.4, hematocrit 34%, RBC 3.42, WBC 1,500, reticulocytes 0.5%, platelets 54,000 and the uncorrected sedimentation rate increased to 56 mm.

On December 26, 1963, 11 days post radiation, the patient refused re-admission to CGH, but agreed to continue the follow-up on an out-patient basis.

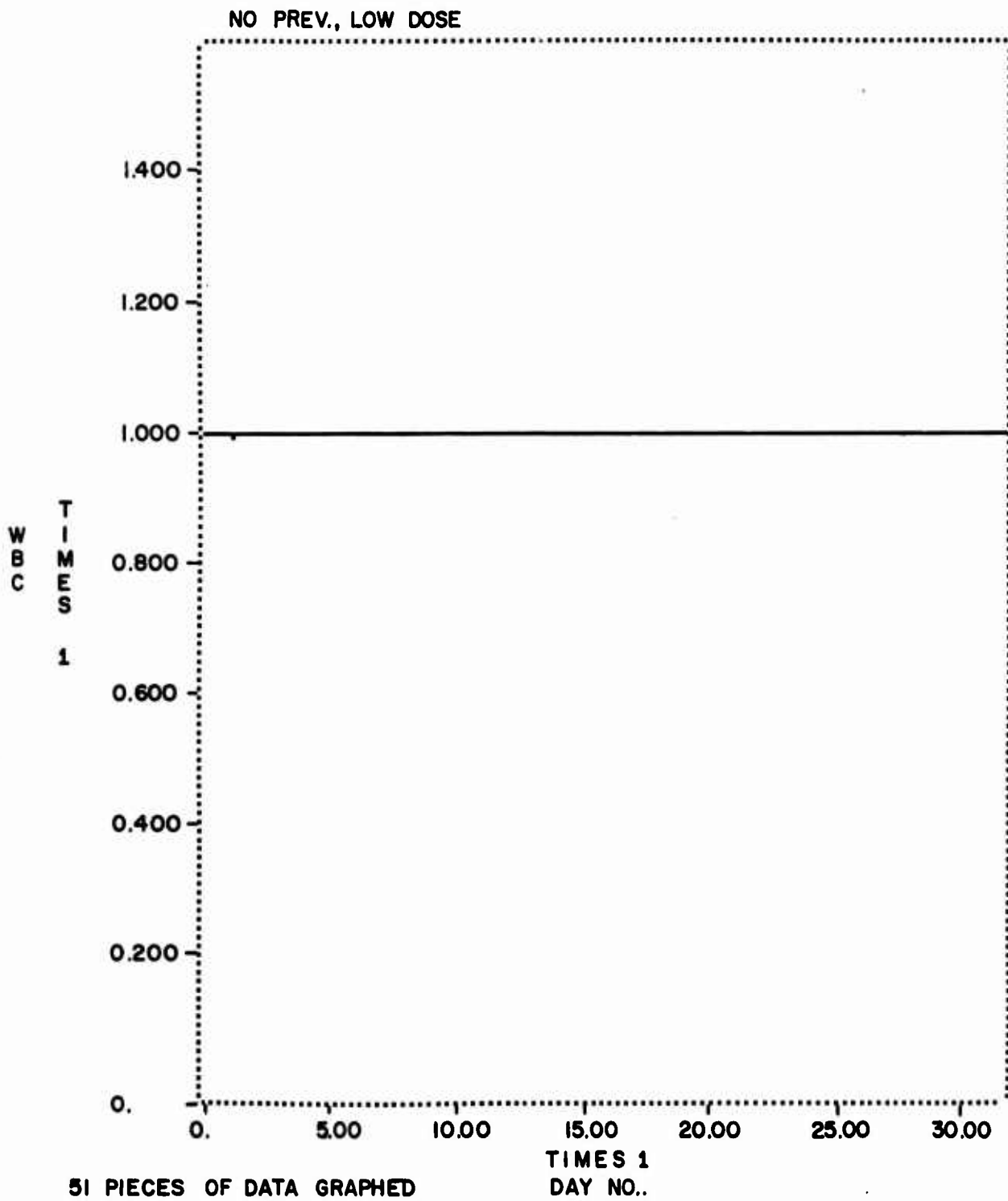
Study No. 037 (continued)

However, on January 10, 1964, 27 days post treatment, he elected to withdraw completely from the study. His hematology values at that time were: hemoglobin 10.2, hematocrit 32%, RBC 3.56, WBC 1,100 (6% polys, 88% lymphs, 6% monos), reticulocytes 0.4%, platelets 35,600, sedimentation rate 75 mm.

He expired February 6, 1964. No autopsy was obtained.



**Fig. 2 PRINTOUT OF TOTAL WHITE COUNT -
NO PREVIOUS THERAPY, LOW DOSE**



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<p>These studies are designed to obtain information which is necessary to estimate combat effectiveness of troops and to develop methods of diagnosis, prognosis, prophylaxis and treatment of radiation injury. At the present time parameters of active investigation are clinical findings, hematologic effects, profile scores, miscellaneous laboratory tests, deoxycytidine excretion in the urine, xanthurenic acid excretion in the urine, chromosome changes in leucocytes, immunologic studies and the use of autologous bone marrow.</p> <p>Six patients were given from 149r to 231r (100-150 rad) total body irradiation from a Co⁶⁰ source. Only one of the patients had prodromal nausea and vomiting with nausea lasting 48 hours. The lowest hematologic values were found 25 to 35 days after irradiation.</p> <p>Deoxycytidine was found in increased amounts in the urine from patients after total body irradiation. In rats much larger amounts were found in the urine after 500r and 800r whole body irradiation than after lesser doses.</p> <p>Studies by Dr. Anthony Luzzio, U.S. Army Research Laboratory, Ft. Knox, Kentucky, indicate there may be an immunologic post irradiation alteration in human gamma globulin antigenicity.</p> <p>Combat effectiveness would be relatively maintained with an exposure up to 200 rad, though a second exposure would result in significant troop ineffectiveness.</p>		

14. KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Irradiation of human patients Metabolic changes Total body irradiation Hematologic effects Deoxycytidine excretion Chromosome changes Endoreduplication Immunologic studies						

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